were loaded as follows (from left to right): lanes 1-4: each 2 μg BMP-2, EHBMP-2, T3 (SEQ ID No.5), and T4 (SEQ ID N0.6); lanes 5-8: each 5 μg BMP-2, EHBMP-2, T3, T4.

Please replace the paragraph beginning on page 30, line 20, with the following replacement paragraph:

The comparison shows that at low concentrations T3 is more effective than BMP-2 (Table 1). In the case of implantation of 1 μg of BMP-2, bone formation was not observed in any of the nine tests, whereas bones were formed in four out of four implanted animals at the same amount of T3. T3 induced bone formation even in three of four animals using only 0.4 μg.

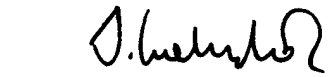
REMARKS

Applicants request entry of this amendment under 37 C.F.R. 1.115(a). This amendment corrects units of measure in the specification that were incorrectly translated from the original German PCT application PCT/EP00/00637 and thus contains no new matter.

Attached hereto is a marked-up version of then changes made to the specification by the amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning on page 4, line 23, has been amended as follows:

Thus, there is a general interest in members of the TGF-β superfamily and their variants with altered biological properties. Kubler et al. (1999) describe a BMP analog EHBMP-2 the primary structure of which differs from that of naturally occurring human BMP-2 in that the first twelve amino acids, which are considered responsible for the strong heparin binding of BMP-2, are replaced by the first thirteen amino acids of human interleukin-2. This genetically altered BMP-2 analog was recombinantly expressed in *E. coli*. EHBMP-2 reveals a negligible affinity to heparin and a higher biological activity in various cell cultures, i.e. *in vitro*. In comparing the *in vivo* activity of the variant with that of natural BMP-2, it was shown that in mouse at BMP-2 concentrations starting from 4 μ[m]g a heterotopic bone induction was produced in nearly all samples, whereas it took an amount of 40 μ[m]g of EHBMP-2 to achieve the same effect. Furthermore, it was found that the resulting extent of new bone formation at the same protein concentrations was significantly greater in natural BMP-2 than its BMP analog, EHBMP-2.

The paragraph beginning on page 23, line 15, has been amended as follows:

Distribution of polypeptide variants within the matrix may or may not be homogenous, but a homogenous distribution would be preferable. The distribution of polypeptide variants may be advantageously configured, depending on the size of the defect or the duration of the healing process. The polypeptide variant concentration within the carrier should range from about 100 μ[m]g/cm^3 to about 2 mg/cm^3, preferably from 250 μ[m]g/cm^3 to 750 μ[m]g/cm^3, and particularly preferably from 450 μ[m]g/cm^3 to 550 μ[m]g/cm^3. As a rule, a concentration of about 500 μ[m]g/cm^3 is used.

The paragraph beginning on page 24, line 15, has been amended as follows:

Fig. 2 shows the picture of a Coomassie Blue-stained SDS polyacrylamide gel after separation of variants T3 and T4 as expressed in *E. coli* and then purified, as well as of BMP-2 and EHBMP-2 in oxidized form (above) and reduced form (below). On the left are the molecular weight standards (15, 20, 30, 35, 68, and 94 kD). The gels were loaded as follows (from left to right): lanes 1-4: each 2 μ[m]g BMP-2, EHBMP-2, T3 (SEQ ID No.5), and T4 (SEQ ID N0.6); lanes 5-8: each 5 μ[m]g BMP-2, EHBMP-2, T3, T4.

The paragraph beginning on page 30, line 20, has been amended as follows:

The comparison shows that at low concentrations T3 is more effective than BMP-2 (Table 1). In the case of implantation of 1 μg of BMP-2, bone formation was not observed in any of the nine tests, whereas bones were formed in four out of four implanted animals at the same amount of T3. T3 induced bone formation even in three of four animals using only 0.4 μ[m]g.